

**ESPS Peer-review Report**

**Name of Journal:** World Journal of Gastroenterology

**ESPS Manuscript NO:** 5451

**Title:** Impaired balance of Th17/Treg cells in carbon tetrachloride- induced liver fibrosis in mice

**Reviewer code:** 00053111

**Science editor:** Cui, Xue-Mei

**Date sent for review:** 2013-09-09 17:32

**Date reviewed:** 2013-09-14 10:05

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

**COMMENTS TO AUTHORS**

Dear Editor: The authors investigated the effect of Th/Treg cells on hepatic fibrosis in CCl<sub>4</sub> mice model and its possible mechanism. They found that Th/Treg imbalance exists in mice with liver fibrosis, and potentially plays a role in the occurrence and development of liver fibrosis via promotion of HSC activation. It was interesting to know that the balance between Th/Treg cells plays a role in the progression of liver fibrosis and interaction between HSC and specific lymphocyte population may give some mechanical insight. However, there are some concerns in the quality of data. 1) The quality of histopathology (Fig. 1) is unacceptably poor. The focuses do not match, and color and darkness are inconsistent. Are these all in same magnification? 1C does not seem to have any fibrosis. 1A and 1C barely see the histology. This reviewer has strong doubt that these livers really have fibrosis or not. Otherwise the data indicated might simply due to the effect of CCl<sub>4</sub>. The authors should show that fibrosis progressed gradually through 4, 8, and 12 weeks using appropriate method. 2) The FACS data in Fig.3 does not have proper control. Theoretically some mice should be injected with olive oil at the same time of CCl<sub>4</sub> injection, and these control data could be briefly shown in the text. 3) In Fig.3, how many numbers of mice gave the percentage of Th/Treg? The figure seems to be from one representative mouse. This should be described. 4) The quality of Fig. 5A is not good. The deceased? density of alpha-SMA in lane 3(+Treg) could be caused just by insufficient blotting or staining. This figure should be replaced to better one to convince readers.

**ESPS Peer-review Report**

**Name of Journal:** World Journal of Gastroenterology

**ESPS Manuscript NO:** 5451

**Title:** Impaired balance of Th17/Treg cells in carbon tetrachloride- induced liver fibrosis in mice

**Reviewer code:** 00504648

**Science editor:** Cui, Xue-Mei

**Date sent for review:** 2013-09-09 17:32

**Date reviewed:** 2013-09-18 22:39

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of	<input type="checkbox"/> No records	
<input type="checkbox"/> Grade D (Fair)	language polishing	BPG Search:	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

**COMMENTS TO AUTHORS**

why was olive oil used and not another oil?

## ESPS Peer-review Report

**Name of Journal:** World Journal of Gastroenterology

**ESPS Manuscript NO:** 5451

**Title:** Impaired balance of Th17/Treg cells in carbon tetrachloride- induced liver fibrosis in mice

**Reviewer code:** 02444760

**Science editor:** Cui, Xue-Mei

**Date sent for review:** 2013-09-09 17:32

**Date reviewed:** 2013-09-20 00:43

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

The manuscript of 'Impaired balance of Th17/Treg cells in carbon tetrachloride induced liver fibrosis in mice' investigates Th17/Treg balance during liver fibrosis, and then its effect on hepatic stellate cell (HSC) function. Some interesting results have been demonstrated that elevated Th17/Treg ratio features the CCl<sub>4</sub>-induced fibrogenesis in rat. This imbalance of T cell subpopulations is accompanied by high-levels of hepatic IL-6, TGF- $\beta$  and  $\alpha$ -SMA. Co-culture of HSCs and Th17 cells, instead of Treg, promotes the expression of  $\alpha$ -SMA, which usually characterizes the transdifferentiation from HSCs to myofibroblasts. These findings, therefore, may uncover novel mechanisms underlying the correlation between immune response and hepatic fibrosis. Major comments 1. According to the manuscript, there are plentiful results concerning Th17/Treg ratio, hepatic expression of inflammatory cytokines, and HSCs activation. However, causality among these facts may not be persuasive to the reviewer. Firstly, authors should make it clear whether the increase in Th17 cells, and also the decrease in Treg cells, leads to the up-regulation of IL-6 and TGF- $\beta$ . Then clear evidence is needed to explain the origination of hepatic  $\alpha$ -SMA. Are they derived from the activated HSCs? Finally, the stimulatory effect of inflammatory cytokines on  $\alpha$ -SMA expression still remains to be elucidated. Minor comments 1. Most figures in the manuscript are presented with low quality. For example, there seems to be great difference in the image acquisition of figure 1. Moreover, the reviewer does not be able to find panel B and F in legend of figure 5. Besides, magnification should be indicated to each panel of each figure. Some figures of western blot are contaminated. They may not meet the criteria of publication. 2. English expression of the manuscript is relative poor, such as 'In model group, there were different degrees of fibroplasias, degeneration and necrosis; the protein levels of IL-6, TGF- $\beta$  and  $\alpha$ -SMA in liver tissue were significantly higher than that of the control group at 12 weeks ( $P < 0.05$ );



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comparing with the control group ,the frequency of Th17 cells in model group were increased but the frequency of Treg cells were decreased, furthermore, there were significantly difference in the amount of Th17 and Treg cells between 4,8 and 12weeks( $P < 0.05$ ). In vitro experiment, Th17 cells promoted, whereas Treg cells inhibited the expression of  $\alpha$ -SMA compared with the control group'. Linguistic improvement, preferably by native speaker, is strongly suggested. 3. There are also some mistakes in Methods and Results. For example, 'The degree of fibrosis was assessed based on Scheuer's scoring system'. But where is the result of fibrosis scoring?